Inventor(s): Axel ULLRICH et al. Appl. No.: 09/977,261 GCGCCCCTGAGCAGAAACAGGAAGAACCAGGCTCGGTCCAGTGGCACCCAGCTCCCTACCTCCTGTGCCAGCCGCCTGGCCTGTGGCA 180 MAGR Small G S L V S W R A F H G C D S A E E L P R V S P R F L R A W H Small CCCCTCCCGTCTCAGCCAGGATGCCAACGACGCCCTGGGCCCCCGGCACCCAGTGTATCACCAAATGCGAGCACACCCCGCCCCAAGCCAG 450 PPP V S A R M P T R R W | A P G T Q C I T K C E H T R P K P KpnI Stul GGGAGCTGGCCTTCCGCAAGGGCGACGTGGTCACCATCCTGGAGGCCTGCGAGAACAAGAGCTGGTACCGCGTCAAGCACCACCACCAGTG 540 SH 3 G E L A F R K G D V V T I L E A C E N K S W Ý R V K H H T S Pvull GACAGGACCCCTGCTCCCAGCTCCCGCGCTGCCCGAGCCCCGAGCCCCTCTCCCCCAACCTCAGCCTCATGCCCTCGTTCCACC 630 G Q E G L L A A G A L R E R E A L_I S A D P K L S L M P_IW F H Pvul I Pst I CGAAGATCTCGGGCCAGGAGGCTGTCCAGCAGCTGCAGCCTCCCGAGGATCGGCTGTTCCTGGTGCGGGAGTCCGCGCGCCACCCCCGGCG 720 G K I S G Q E A V Q Q L Q P P E D G L F L V R E S A R H P G SH 2 Clai ACTACGTCCTGTGCGTGAGCTTTGGCCGCGACGTCATCCACTACCGCGTGCTGCACCGCGACCGCCACCTCACAATCGATGAGGCCGTGT 810 D Y V L C V S F G R D V I H Y R V L H R D G H L T 1 D E A V TCTTCTGCAACCTCATGGACATGGTGGAGCATTACAGCAACGACAACGGCCCTATCTGCACCAACCTGGTGAGACCAAACCGGAAACACG 900 F F C N L M D M V E H Y I S K D K G A I C T K L V R P K R K H

Title: NOVEL

TYROSINE KINASES

MEGAKARYOCYTIC PROTEIN

FIG.1A

Title: NOVEL MEGAKARYOCYTIC PROTEIN TYROSINE KINASES Inventor(s): Axel ULLRICH et al. Appl. No.: 09/977,261 Pstl GGACCAAGTCGGCCGAGGAGGAGCTGGCCAGGGCGGGCTGGTTACTGAACCTGCAGCATTTGACATTGGGAGCACAGATCGGAGAGGGAG 990 G T K S A E E E L A R A G W L L N L_IQ H L T L G A Q I G E G Stul **PSTI** AGTTTCGAGCTGTCCTGCAGCGTGAGTACCTGGGGCAAAAGGTCGCCGTGAAGAATATCAAGTGTGATGTGACAGCCCAGGCCTTCCTGG 1080 E F G A V L Q G E Y L G Q K V A V K N I K C D V T A Q A F L TK ACGAGACCGCCGTCATGACGAAGATGCAACACGAGAACCTCGTGCGTCTCCTGGGCGTGATCCTGCACCAGGGGCTGTACATTGTCATGG 1170 DETAVMIKMQHENLVRLLGVILHQGLYIVM Small Psll AGCACGTGAGCAACGGCAACCTGGTGAACTTTCTGCCGACCCCGGGTCGAGCCCTCGTGAACACCCCTCAGCTCCTGCAGTTTTCTCTGC 1260 E H V S K G N L V N F L R T R G R A L V N T A Q L L Q F S L HinDIII ACGTGCCCGAGGCCATCGAGTACCTGCAGAGCAAGAAGCTTGTGCACCGCGACCTGGCCGCCGCAACATCCTGGTCTCAGAGGACCTGG 1350 HVAEGMEYLESKKLVHRDLAARNILVSEDL TGGCCAAGGTCAGCGACTTTGGCCTGGCCAAAGCCGAGCGGAAGCGGCTAGACTCAAGCCGGCTGCCCGTCAAGTGGACGGCCCCCGAGG 1440 V A K Y S D F G L A K A E R K G L D S S R L P V K W T A P E Ndel CTCTCAAACACCCGAAGTTCACCAGCAAGTCCGATGTCTGGAGTTTTGGGGTGCTGCTGGGAGGTCTTCTCATATGGACCGGGTCCCGT 1530 A L K H G K F T S K S D V W S F G V L L W E V F S Y G R A P Kpnl ACCCTAAAATGTCACTGAAAGAGGTGTCGGAGGCCGTGGAGAAGGGGTACCGCATGGAACCCCCGGAGGGCTGTCCAGGCCCCGTGCACG 1620 Y P K M S L K E V S E A V E K G Y R M E P P E G C P G P V H.. Pvull Sma I TCCTCATGAGCAGCTGCTGCGCAGGCAGAGCCCGCCGCCGCCGCCACCCTTCCGCAAACTGGCCGAGAACTGGCCCGGGAGCTACGCAGTG 1710

Y L M S S C W E A E P_I A R R P P F R K L Ā E K L_I A R E L R S

MEGAKARYOCYTIC PROTEIN

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

Appl. No.: 09/977,261



CAGGTGCCCCAGCCTCCGTCTCAGCGCAGGACGCCGACGCTCCACCTCGCCCCGAAGCCAGGAGCCCTGACCCCACCCGGTGGGGCCCT

A G A P A S V S G Q D A D G S T S P R S Q E P

TGGCCCCAGAGGACGGAGAGAGTGGAGAGTGCGGGGGGCCACTGACCAGGCCCCAAGGAGGGGGGGAAGTCATCCTCCTGG

1890
TGCCCACAGCAGGGGGGGCCCCCCCCCGTAGGGGGCCCTCTGGGGGCCCGTGGACACCCCCAGACCTGCGAAGGATGATCGCCCGATAAAGACGG

1980

FIG.1C

ATTCTAAGGACTCTAAAAAA 2000

MEGAKARYOCYTIC PROTEIN 177261 160702 TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.



CCCCTTTTTCCTTAGAGCTTGAGAGTCAAAG	ACGACCCACATGTATACTTCCGCTCTAGCGAGT	AGGATGATAATATGGATACA	90
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	180	TTTG / L																												
	270	STGTG	GATG	TCA	W	VAG/	\TT#	AA	ATTO	TCC.	CGA	AAA	:AGA	AGC	GGC	ACC	AAA	ATG	AAA	GAC	TAT	GAA	TAT	TAC	TCC	CT	VAA(VAC#	CAA	AC
PH	360	ATGCA Y A	TCTA	TATG	CTC	2110	GG(SATO	1 AA(TAT	GTC	ATI	CAG	111	CCA	TAC	CAG	AGA	GAG	GTA	CCI	ACG	CAG	GAC	GAC	CTO	\AA	\GT/	GAA	GA
	450	CTCCC S_C	ATAG	TACC	aag'	STC	CTG	CTG	CAC	CCC	AAC	CG	VAGO	:ATA	GAC	AAA	CAA	TT.	GC/	SAA	STIC	TGC	CAC	VAG1	CCG/	GAG	4GA(rga/	AAA	TC
	540	TGCAT L_H	MTC1	CCTA	TAT	GCA	GAM	TGG	CTC	ACC	NTGT	CC	CCCA	\GC(GC/	`AAA	TGI	AGO	CAC	CCAC	TGO	TGI	CTC	3110	SAAC	CCC	GGA(CT(CTI	11
	630	TGGAT	VAAA'	CTCA	GTT	CCT	GTT	GCA	CCC	CC1	SATA	SAA	CCTO	AGT(:AG/	GAC	CCA	:110	CACO	TCCO	\GT	CAGA	ACA(SAA	NGA(TGA	CAA	AGT	TGC	AC
SH3	720	M D GTCTA	ACCA(AGT/	TCA	ICI	CCA	CCA	CAG	:TC(TGG(CTA	AAA	i Gaa	VAA(\TC/	ŒAZ	. .AA([GA(ΑΤΑ	CCA	VGC(TCT.	CAC	TAC	aag	TTC	ATC	:AC(GC
วทว	810	S L SACTGG	CCTG	TTC	GAC	GAA	AGG	CCA	ATT	TAT	GCA	CAT	CAA	CTT	\AA	GCC/	CCA	CTC	TGG(CTA	AAT	ı SAA	AAA	CTC	CAA	CAG	TGA	ATA	CC/	G
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	990	T S ICCAGA																												
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SH4		V S CCAGAA	Ţ	Υ	M	G	٧	Q	<u>S</u>	<u>S</u>	N	R	l V	, N	F	A	G	E	K	G	K	Q	R	L	<u>L</u>	(<u> </u>) <u>S</u>	S	_
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Title: NOVEL MEGAKARYOCYTIC PROTEIN TYROSINE KINASES Inventor(s): Axel ULLRICH et al. Appl No · 09/977.261

A AC	TAC	TGT	Ш	GAT	TCC	ATT	CCA	AAG	CTT	ATT	CAT	TAT	CAT	CAA	CAC	:AAT	TCA	GCA	CGC	ATG	ATC	AC/	CCC	CTC	CGC	CAC	CCT	ĠTG	TCA'	1260	
N	Υ	С	F	D	<u>S</u>	<u> </u>	P	K	L	I	Н	Y	Н	Q	Н	N	S	A [*]	G	M	I	Ī	R	L	R	H	P	٧	S		
					CTC V																-					_			CTG L	1350	
					TGGA G												-	-	-	-				-	-			-		1440	
					ICAC Q																								TAC Y	1530	
					GACT T																				-					1620	T
					CGAT D			-																					CTIG L	1710	
					CTGT C																								AAAG K	1800	
					STCA S																								CTGG W	1890	
					CCCC G																								CCCG R	1980	
					GCÀC D																								CCTG	2070	
			_		ACTI L							TGA	AG/	VAG <i>I</i>	\AA`	TTAC	GAG	STG	CTG	ATA	¥GA.	ATG	AA T.	ATA	GAT	GCT	GGC	CAG	CATT	2160	
Ħ	CAT	[CA]	TT!	ΓΑΑ	CGA	VAG 1	[AG(CAAC	GCA	ATAA	\TG1	TAAT	11/	VGC1	[AG	1113	TA	ATA	GTG	TTC	ICT	GTA	TTG	TCT	ATT	ATT	TAG	AAA	TGAA	2250	
CA	ACG	CAGO	SAA	\CA	AAA(CAT	ICC(CTT(SAA	ATTI	AGO	TCA	(AA)	TA(STA	ATT	TGT	ITT.	ATG	CTG	CCC	CTG	ATA	TAA	CAC	Ш	CCA	GCC	TATA	2340	
GC	AGA	4GC/	ACA	m	TCAC	SAC	rgc.	AAT	ATAC	GAGA	CTC	STGT	TC	ATG	(GT	AAA (GAC1	IGA	GCA	GAA	CTG	AAA	AAT	TAC	TTA	TTG	GAT	ATT	CATT	2430	
CT	H	CII	TATA	ATTO	GTC/	ATT(STC.	ACA.	ACA/	ATT/	LAA1	TAT/	CT/	ACC/	AAG	TAC	AAA/	AAA	AAA.	AAA.	AAA	AAA	AA	25	nn						

MEGAKARYOCYTIC PROTEIN 9 9 7 7 2 6 1 ... 0 6 0 7 0 2

TYROSINE KINASES

CCCGACTGGTCGAAAGACAGGAACAGACTTGAAACAGGGGGAGACCTCCTCGCGAAACGAAGACGTGGAGGTTTTACCAGGGATAAGAAG	"30» (25%, 2
AAAAGACACCTTCCTAGTGAGCAGCTGCCCAGCTCCTGCTCAGTTTTGCCTCGGGGTAGCACCTCCAGCCACAGAAAGCAAAGCCAAGCCGGTAAG	180
TCTCTCCAGGTAGGACTTGCTGCAACCCAGCTGCTGGACTGATCTGAAACGCGACTTTGCATACTCTCCGAAGTATCGTGAGTTGGTGCT N V S W C	270
GACTTCAAAGTTGCCTCGTGAAGGAAGATAACGTCGATCGCAGAGACTAAGGGGAGAGGGGAGAAGCCCTGCTCCTCTTCTCCCCACCAAG	360
GCACAATGAGCAACATCTGTCAGAGCCTCTCGGAGTACCTAGAACCCTATCTCCCCTGTTTGTCCACGGAGGCAGACAAGTCAACCGTGA M S N I C Q R L W E Y L E P Y L P C L S T E A D K S T V	4 50
TIGAAAATCCAGGGGGCCTTIGCTCTCCCCAGTCACAGAGGCATGGCCACTACTTIGTGGGCTTTGTTTGATTACCAGGCTCGGACTGCTG I E N P G A L C S P Q S Q R H G H Y F V A L F D Y Q A R T A	540
AGGACTTGAGCTTCCGAGCAGGTGACAAACTTCAAGTTCTGGACACTTTGCATGAGGGCTGGTGGTTTGCCAGACACTTGGAGAAAAGAC E D L S F R A G D K L Q V L D T L H E G W W F A R H L E K R	630 SH 3
GAGATGGCTCCAGTCAGCAACTACAACGCTATATTCCTTCTAACTACGTGGCTGAGGACAGAAGCCTACAGGCAGAGCCGTGGTTCTTTG R D G S S Q Q L Q G Y I P S N Y V A E D R S L Q A E P W F F	720
GAGCAATCGGAAGATCAGATGCAGAGAAACAACTATTATATTCAGAAAACAAGACCGGTTCCTTTCTAATCAGAGAAAGTGAAAGCCAAA G A I G R S D A E K Q L L Y S E N K T G S F L I R E S E S Q	810 SH 2
AAGGAGAATICTCTCTTTCAGTTTTAGATGGAGCAGTIGTAAAACACTACAGAATTAAAAGACTGGATGAAGGGGGATTTTTTCTCACGC K G E F S L S V L D G A V V K H Y R I K R L D E G G F F L T	900
GAAGAAGAATCTTTTCAACACTGAACGAATTTGTGAGCCACTACACCAAGACAAGTGACCGCCTGTGTGTCAAGCTGCGGAAACCATGCT R R R I F S T L N E F V S H Y T K T S D G L C V K L G K P C	990
TAAAGATCCAGGTCCCAGCTCCATTTGATTTGTCGTATAAAACCGTGGACCAATGGGAGATAGACCGCAACTCCATACAGCTTCTGAAGC L K I Q V P A P F D L S Y K T V D Q W E I D R N S I Q L L K	1080
GATTGGGATCTGGTCAGTTTGGCGAAGTATGGGAAGGTCTGTGGAACAATACCACTCCAGTAGCAGTGAAAACATTAAAACCAGGTTCAA R L G S G Q F G E V W E G L W N N T T P V A V K T L K P G S	
TGGATCCAAATGACTTCCTGAGGGAGGCACAGATAATGAAGAACCTAAGACATCCAAAGCTTATCCAGCTTTATGCTGTTTGCACTTTAG M D P N D F L R E A Q I M K N L R H P K L I Q L Y A V C T L	1260

MEGAKARYOCYTIC PROTEIN 9 9 7 7 2 6 1 . 0 6 0 7 0 7

TYROSINE KINASES

		MKK1	MKK2
HUMAN	·		
MEG/ERYTH	MEG-01 K562 MO7E HEL	+++ ++ ++ +++	+++ + ++
MYELO/MAC	KG-1 HL-60 TF-1	+ + + .	++ + +
B-CELL	ALL-1 RAJI DAUDI	 	+ - -
T-CELL	MOLT-3 JURKAT	- -	Ξ
EPITHELIAL	HELA	-	-
RODEN	T		
,	BM SPLEEN THYMUS LIVER BRAIN	+ +++ - +	++++
RAT NEURAL	P19	+	_

MEGAKARYOCYTIC PROTEIN 9 7 7 2 6 1 . 0 6 0 7 0 2

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

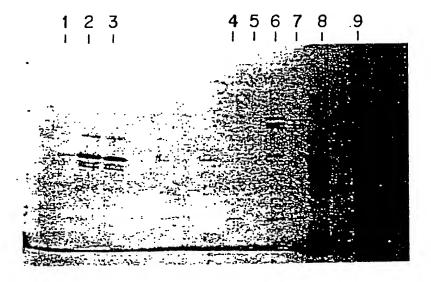


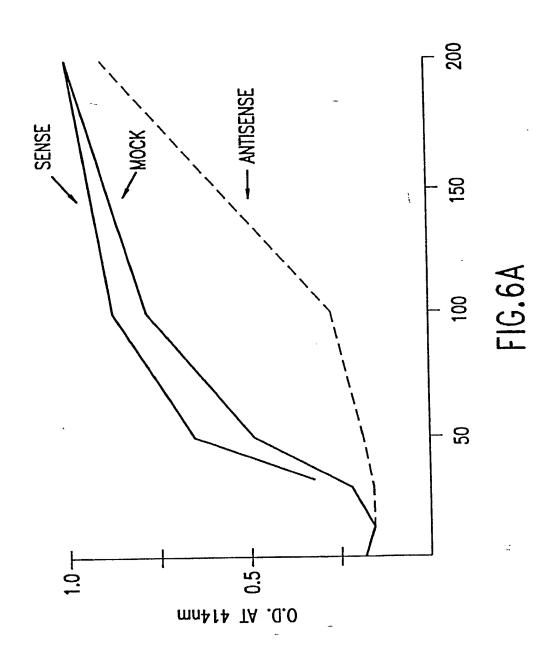
FIG. 5

Title: NOVEL

MEGAKARYOCYTIC PROTEIN G F F E E L C E C F E E

TYROSINE KINASES

TYROSINE KINASES
Inventor(s): Axel ULLRICH et al.
Appl. No.: 09/977,261



MEGAKARYOCYTIC PROTEIN 977261.060702

TYROSINE KINASES Inventor(s): Axel ULLRICH et al. Appl. No.: 09/977,261

MKKI PROTEIN EXPRESSION

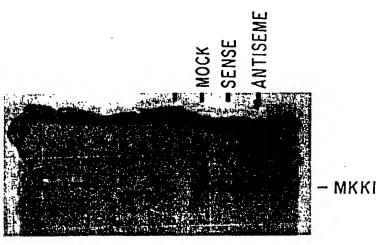


FIG. 6B

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

Appl. No.: 09/977,261

MKK2 MKK3

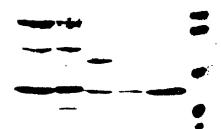


FIG. 7

MEGAKARYOCYTIC PROTEIN19077861.06070E

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

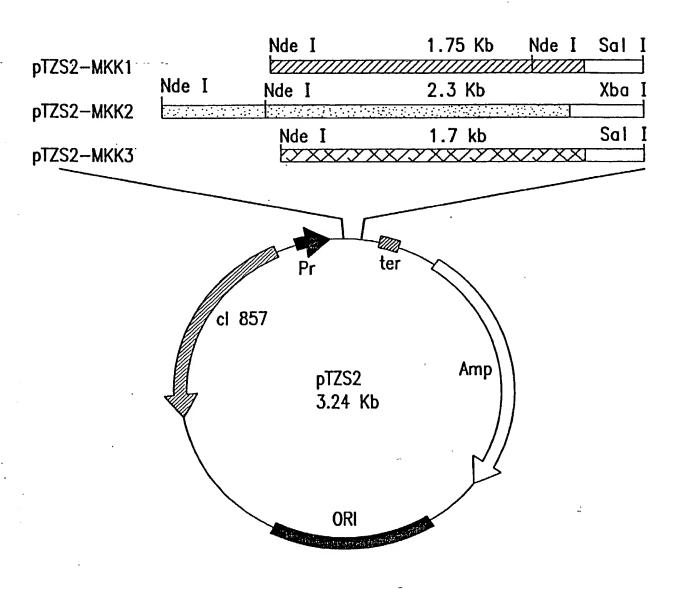


FIG.8

TYROSINE KINASES

1	M A G R G S L V S W R A F H G C D S A E E L P R V S P R F L M S A I Q A A	MKK-1 aa h hCSK (JH0559)
31 8	RAWHPPPVSARMPTRRWAPGTOCITKCEHT	MKK1 aa hCSK (JH0559)
61 22	R P K P G E L A F R K G D V V T I L E A C E N K S W Y R V K G T A E Q D L P F C K G D V L T I V A V T K D P N W Y K A K	MKK1 aa hCSK (JH0559)
91 52	HHTSGQEGLLAAGALREREALSADPKLSLM NKV-GREGIIPANYVQKREGVKAGTKLSLM	MKK1 aa hCSK (JH0559)
121 81	PWFHGKISGQEAVQQLQPPEDGLFLVRESA PWFHGKITREQAERLLYPPETGLFLVREST	MKK1 aa hCSK (JH0559)
151 111	RHPGDYVLCVSFGRDVIHYRVLHRDGHLTINYPGDYTLCVSCDGKVEHYRIMYHASKLSI	MKK1 aa hCSK (JH0559)
181 141	DEAVFFCNLMDMVEHYSKDKGAICTKLVRP DEEVYFENLMQLVEHYTSDADGLCTRLIKP	MKK1 aa hCSK (JH0559)
211 171	K R K H G T K S A E E E L A R A G W L L N L Q H L T L G A Q K V M E G T V A A Q D E F Y R S G W A L N M K E L K L L Q T	MKK1 aa hCSK (JH0559)
241 201	I G E G E F G A V L Q G E Y L G Q K V A V K N I K C D V T A I G K G E F G D V M L G D Y R G N K V A V K C I K N D A T A	MKK1 aa hCSK (JH0559)
271 231	Q A F L D E T A V M T K M Q H E N L V R L L G V I L H Q Q A F L A E A S V M T Q L R H S N L V Q L L G V I V E E K G	MKK1 aa hCSK (JH0559)
299 261	G L Y I V M E H V S K G N L V N F L R T R G R A L V N T A Q G L Y I V T E Y M A K G S L V D Y L R S R G R S V L G G D C	MKK1 aa hCSK (JH0559)
329 291	L L Q F S L H V A E G M E Y L E S K K L V H R D L A A R N I L L K F S L D V C E A M E Y L E G N N F V H R D L A A R N V	MKK1 aa hCSK (JH0559)
359 321	L V S E D L V A K V S D F G L A K A E R K G L D S S R L P V L V S E D N V A K V S D F G L T K E A S S T Q D T G K L P V	MKK1 aa hCSK (JH0559)

Title: NOVEL
MEGAKARYOCYTIC PROTEIN TYROSINE KINASES

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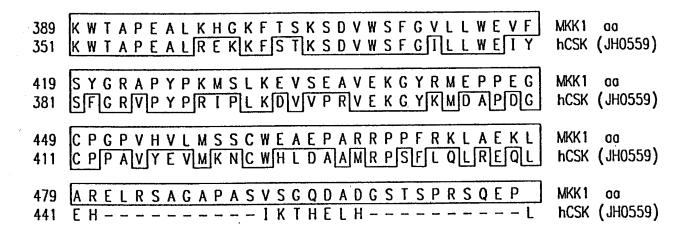


FIG.9B

Title: NOVEL MEGAKARYOCYTIC PROTEING 7 72 6 1 0 6 0 7 0 2 TYROSINE KINASES

1 1 1	MDTKSILEELLLKRSQQKKKMSPNNYKERL MAA-VILESIFLKRSQQKKKTSPLNFKKRL MNNFILLEEQLIKKSQQKRRTSPSNFKVRF MMV	MKK2 ga hAtk (X58957) hTKT (L10717) mTec (X5663)
31 30 31 4	FVLTKINLSYYE YDKMKRGSRKGSIEIK FLLTVHKLSYYEYDFERGRRGSKKGSIDVE FVLTKASLAYFEDRHGKKRTLKGSIELS	MKK2 aa hAlk (X58957) hTKT (L10717) mTec (X5663)
59 60 59 4	K I R C V E K V N L E E Q T P V E R Q	MKK2 aa hAlk (X58957) hTKT (L10717) mTec (X5663)
78 90 70 4	YPFQIVYKDGLLYVYASNEE EQISIIERFPYPFQVVYDEGPLYVFSPTEEISIPCHYKYPFQVVHDNYLLYVFAPDRESFPVKINFHSSPQ	MKK2 aa hAlk (X58957) hTKT (L10717) mTec (X5663)
98 120 98 17	SRSQWLKALQKE I RGNPHLL VKYHSGFF VDLRKRWIHQLKNVI RYNSDL VQKYHPCFWIDSRQRWVLALKEETRNNNSLVPKYHPNFWMDSRDRWVKKLKEE IKNNNN I MIKYHPKFWAD	MKK2 aa hAlk (X58957) hTKT (L10717) mTec (X5663)
128 150 128 47	GOYLCCSOJAKNAMGCOILENRNGSLKPGS	MKK2 aa hAlk (X58957) hTKT (L10717) mTec (X5663)
158 180 149 73	E E K H R V P T F P D R V L K I P R A V P V L K M D A P S S S H R K T K K P L P P T P E E D Q I L K K P L P P E T K N A S K K P L P P T P E D N R	MKK2 aa hAlk (X58957) hTKT (L10717) mTec^(X5663)
188 206 166 89	PAAAPVSTSELKKVVALYD	MKK2 aa hAlk (X58957) hTKT (L10717) mTEC (X5663)

Title: NOVEL MEGAKARYOCYTIC PROTEIN TYROSINE KINASES

Аррі. № 09/9/7,201	一覧 (時) 一种事。
218 SNSKKIYG SQPNFNMQY IPREDFP-DWWQ V 225 YMPMNAND LQLRKGDE YFI LEESNLPWWRA 182 YQINDPQELALRRNEE YCLLDSSE IHWWRV 108 FQATEAHDLRLERGQE YIILEKNDLHWWRA	MKK2 aa hAtk (X58957) hTKT (L10717) mTec (X5663)
247 RKLKSSSSSEDVASSNQKERNVNHTTSKIS 255 RDKNGQEGYIPSNYVTE-A 212 QDRNGHEGYVPSSYLVEKS 138 RDK	MKK2 aa hAtk (X58957) hTKT (L10717) mTec (X5663)
277 WEFPESSSSEEEENLDDTDWFAGNISRSQS 273EDSIEMYEWYSKHMTRSQA 231PNNLETYEWYNKSISRDKA 141YGWYCRNTNRSKA	MKK2 aa hAtk (X58957) hTKT (L10717) mTec (X5663)
307 EQLLRQKGKEGAFMVRNSSQVGMYTVSLFS 292 EQLLKQEGKEGGFIVRDSSKAGKYTVSVFA 250 EKLLLDTGKEGAFMVRDSRTAGTYTVSVFT 154 EQLLRTEDKEGGFMVRDSSQPGLYTVSLYT	MKK2 oo hAtk (X58957) hTKT (L10717) mTec (X5663)
337 K - AVNDKKGTVKHYHVH IN A ENKLYL A E 322 K S T - G D P Q G V I R H Y V V C S T P Q S Q Y Y L A E 280 K A V V S E N N P C I K H Y H I K E T N D N P K R Y Y V A E 184 K F G - G E G S S G F R H Y H I K E T A T S P K K Y Y L A E	MKK2 aa hAtk (X58957) hTKT (L10717) mTec (X5663)
364 NYCFDSIPKLIHYHQHNSAGMITRLRHPVS 349 KHLFSTIPELINYHQHNSAGLISRLKYPVS 310 KYVFDSIPLLINYHQHNGGGLVTRLRYPVC 213 KHAFGSIPETIEYHKHNAAGLVTRLRYPVS	MKK3 aa hAlk (X58957) hTKT (L10717) mTec (X5663)
394 TKANK VPD SVSL GNG I WELKREE I TLL KEL 379 Q Q NKN APST A G L G Y G SWE I D PKDL TF L KEL 340 F G R Q K A P V T A G L R Y G K WVI D P S E L T F V Q E I 243 TKGKN A P T T A G F S Y D K W E I N P S E L T F M R E L	MKK2 aa hAtk (X58957) hTKT (L10717) mTec~(X5663)
424 G S G Q F G V V Q L G K W K G Q Y D V A V K M I K E G S M S 409 G T G Q F G V V K Y G K W R G Q Y D V A I K M I K E G S M S 370 G S G Q F G L V H L G Y W L N K D K V A I K T I R E G A M S 273 G S G L F G V V R L G K W R A Q Y K V A I K A I R E G A M C	MKK2 aa hAtk (X58957) hTKT (L10717) mTec (X5663)


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E DEFF QE AQ TIMMKL SHPKL VKFIYG V CISIKE Y
                                              MKK2 aa
   E DEFIEEAKVMMNLSHEKLVQLYGVCTKQR
                                              HALK (X58957)
   |E|E|DFIEEA|E|VMMKLSHPKLVQLYGVC|LE|Q|A
                                              hTKT (L10717)
  EEDFIEEAKVMMKLTHPKLVQLYGVCTQQK
303
                                              mTec (X5663)
   MKK2
                                                  aa
   PIFTITTELYMANGCLLNYLREMRHRFQTQQL
                                              hAtk (X58957)
469
   PICLVFEFMEHGCLSDYLRIORGLIFIAAETL
                                               hTKT (L10717)
   PIYIVTEFMERGCLLNFLRQRQGHFSRDML
                                              mTec (X5663)
   MKK2 aa
   LEMCKD V CEAMEY LESKQFLHRDLAARNCL
499
                                               hAtk (X58957)
   L G M C L D V C E G M A Y L E E A C V I H R D L A A R N C L
460
                                               hTKT (L10717)
   |L|S|M C|Q|D V C E G ME|Y L E|R N S|F I H R D L A A R N C L
                                               mTec (X5663)
   V D R D L C V K V S D F G M T R Y V L D D Q Y V S S V G T K
544
                                               MKK2 aa
   VNDQGVVKVSDFGLSRYVLDDEYTSSVGSK
529
                                               hAtk (X58957)
   VGENQVIK V S D F G M T RFT V L D D Q Y T S ST G T K
                                               hTKT (L10717)
490
   V N E A G V V K V S D F G M A R Y V L D D Q Y T S S S G A K
393
                                               mTec (X5663)
   FPVKWSAPEVFHYFKYSSKSD<u>V</u>WAFGILMW
574
                                               MKK2 aa
   FPVRWSPPEVLMYSKFSSKSDIWAFGVLMW
                                               hAtk (X58957)
559
   FPVKWASPEVFSFSRYSSKSDVWSFGVLMW
520
                                               hTKT (L10717)
   FPVKWCPPEVFNYSRFSSKSDVWSFGVLMW
                                               mTec (X5663)
   E V F S L G K Q P Y D L Y D N S Q V V L K V S Q G H R L Y R
                                               MKK2 oa
   E L Y S L G K M P Y E R F T N S E T A E H I A Q G L R L Y R
589
                                               hAlk (X58957)
   EVFSEGKIPYENRSNSEVVEDISTGFRLYK
550
                                               hTKT (L10717)
   ETIFT EIGRM PFEK NT NYE V VIT MVT RIGHR LHR
                                               mTec (X5663)
   PHLASDTIYQIMYSCWHELPEKRPTFQQLL
634
                                               MKK2 aa
   PHLASEKVYTIMYSCWHEKADERPTFKILL
619
                                               hAtk. (X58957)
   PRLASTHVYQIMNHCWKERPEDRPAFSRLL
580
                                               hTKT (L10717)
   PKL ATKYLYE VMLRCWQERPEGRPSFEDLL
                                               mTec (X5663)
   SSIE PLREKDKH
664
                                               MKK2 aa
   SNILDVMDEES
649
                                               hAtk (X58957)
   RQLAELAES----GL
                                               hTKT (L10717)
610
   RTUDELVECEETFGR
                                               mTec (X5663)
```

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MEGAKARYOCYTIC PROTEIN 977261 ... 060712
               TYROSINE KINASES
            Inventor(s): Axel ULLRICH et al.
               Appl. No.: 09/977,261
  MSNICORLWEE -
                                         MKK3 MPI
  MGCVQCKDKEA-T---KLTEERDGSLNQ-S
  cYrk
  MGSNKSKPKDA-SQR-RRSLEPAENVHG-A
                                         hSrc
  MGCIKSKENKS-PAI-KYRPENTPEPVS-T
                                         hYes
  MGCVFCKKLEP-VATAKEDAGLEGDFRSYG
                                          hFqr
  M G C I K S K C K D S L S D D G V D L - K T Q P V R N T E R
                                          hLyn
  hHc k
  MGCGCSS----HPEDDWMENTDVCENCHY
                                          hLck
  MGLLSSKRQVSEKGKGWSPVKIRTQDKAPP
                                          mB1k
                                          MKK3 MPI
11 "
                                                aa
   SGYRYGTDPTPQHYPSFGVTSIPN--YNNF
26
                                          hFyn
26
  PPSQYDPDPTI-QLSGAF--THIPD--FINNF
                                          cYrk
  GGG A F P A S QIT P S K P A S A D G H R G P S A A F A P A
28
                                          hSrc
   S V S HYG A EP TIT V SPC PS SISAK G T A V NF SIS L
28
                                          hYes
   AADHYGPDPTKARPAS-SFAHIPN--YSNF
30
                                          hFgr
  T I Y V R D P T S N K Q Q R P V P E S Q L L P G Q R F Q T K
30
                                          hLyn
  PVY VPD PT STIKPGPNSHNSNTPGIR - - - -
28
                                          hHc k
  PIVPLDGKGTLLIRNGSEVRD-PLVTYEGS
26
                                          hLck
31
  mB1k
   YLPCLSTEADKSTVIENPGALCSPQSQRHG
15
                                          MKK3 MPI aa
54
   HAA---GGQGLTVFGGVN--SSSHTGTLRT
                                          hFyn
   HAA---AVSPPVPFSGPGFYPCNTLQAHSS
51
                                          cYrk
58
   A A A E P - - - - - K L F G G F N S S D T V T S P Q R A G
                                          hSrc
58
  hYes
  SSQAINPG----FF-----LDSGTIRG
57
                                          hFgr
60
   hLyn
54
   E|A|G S - - - - - E D -
                                          hHck
55
   N P P A - - - - - - S P L Q D - - - - - -
                                          hLck
49
                                          mBlk
45
   H----YFVALFDYQARTAEDLSFRAGDK
                                          MKK3
                                             MPI aa
79
   R G G T G V T L F V A L Y D Y E A R T E D D L S F H K G E K
                                          hFyn
   I T G G G V T L F [] A L Y D Y E A R T E D D L S F Q K G E K
78
                                          cYrk
81
   PLAGGVTTFVALYDYESRTETTDLSFKKGER
                                          hSrc
   GLTGGVT[[FVALYDYEART[TEDLSFKKGE]R
88
                                          hYes
74
   V S G I G V T L F I I A L Y D Y E A R T E D D L T F T K G E K
                                          hFgr
66
     ---DIVVALYPYDGI-HPDDLSFKKGEK
                                          hLyn
   60
                                          hHck
          NLVIALHSYEPSHDGDLGFEKGEQ
64
                                          hLck
     55
                                          mBlk
```

MEGAKARYOCYTIC PROTEIN 7 2 5 1 . O 6 0 7 0 2 TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

		: 09/977,261	2 41 · 24 1
69	LOVLDTLHEGWWFAI	HLEKRRDGSSQQLQG	MKK3 MPI aq
109	FOILNSSEGDWWEAL	S LII GE II G	hRyn cYrk
108 111	LQ IVNNTEGDWWLA	S L SSGAT G	hSrc
118	FOIINNTEGDWWEA	13	. hYes
104		S L SSC K T G	hFqr
90	MKVLEEH-GEWWKA	S LILTIKIKĖG – – – – –	hLyn
84	M V VILIE E S -IGIEIW WIKIA I	RS LIAITIRIKIEIGI	hHck
88	LRILEQS-GEWWKA]S [T T G Q E G	hLck
79	LOVLRST-GDWWLA	S L V T G R E G	mBlk
99	YIPSNYVAEDRSLQ	LEPWFF GALL GRISD A EK	MKK3 MPI aa
132	YIPSNYVAPVDSIIQ	A E E W Y F G K L G R K D A E R	•
131	Y I P S N Y V A P V D SIIIQ	A E E W Y F G K T G R K D A E R	cYrk
134	T I P S N Y V A PISID SILIQ	NEEWYFGKIIRRESER	hSrc
141 127		A E E W Y F G K M G R K D A E R A E E W Y F <u>G K I G</u> R K D A E R	hYes hFgr
112	FIPSNYVAKINTITE	TEEWFFKDITTRKDAER	hLyn
106	YIPSNYVARVDSIE	I F F W F F K G I I S R K D A F R	hHck
110	FILPENELV ALK ANS LE	TEEWFFKGUSRKDAER PEPWFFKNLSRKDAER	hLck
101	TVPSNFVAPVETLE	/EKWFFRT[]SRKDAER	mB1 k
129	O L L Y S E N K T G S F L I	RESESOK GEFSLSVLD RESETTKGAYSLSIRD	MKK3 MPI aa
162	Q L LISFIGNPRGITIFLI	RESETTKGAYSLSIIRD	
161 164	THE NEW GILLET	RESETTKGAYSLS[[RD] RESETTKGAY[C]LSV[S]D	cYrk hSrc
171	THE LINE CHORCLE LIV	RESETTKGAYSLS[[RD]	
157	O LISP GN POGAFIT	RESETTKGAYSLSURD	hLyn
142	QLLAPGNSAGAFLI	RESETÜK GSFSLSVRD	hHck
136	QLLAPGNMLGSFMI	RDSETTKGSYSLSVRD	hHck
140	QLLAPGNTHGSFLI	RESESTAGSFSLSVRD	hLck
131	QLLAPMNKAGSFLI	RESESNKGAFSLSVKD	mBlk
455			· ·
159		KRL DEGGFFLTRRR IF RKLDNGGYYITTRAQF RKLDSGGYYITTRAQF RKLDSGGFYITSRTQF	MKK3 MPI aa
192 191	WDEAKGDHVKHYKI	K L D N G G Y Y I I I R A Q F	hFyn
194	EUMYKCI MAKHAKI	K L DISIG G T T I I I K A Q F	cYrk hSrc
201	WDEIRGDNVKHYKI	RKLDNGGYYITTRAQF	hYes
187	WDQTRGDHVKHYKI	RKLDMGGYYITTRVQF	hFgr
172	FDPVHGDVIKHYKI	RSLDNGGYYISPRITF	hLyn
166	YDPRQGDTVKHYKI	RITILDNGGFIYIISPRISTIF	hHck
170	FDQNQGEVVKHYKI	RINILDNGGIFIYIISPIRIITIF	
161	ITT-QGEVVKHYKI	RSLDNGGYYISPRITE	mBlk ——

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MEGAKARYOCYTIC PROTEIN OFFFEE L.OSOFOE
                TYROSINE KINASES
             Inventor(s): Axel ULLRICH et al.
                Appl. No.: 09/977,261
   STLNEFVSHYTKISDGLCVKLGKPCLK1QV
                                               MKK3 MPT
184
   EIT L QQE V Q H Y SE RAAG L CCR L V V P CH KGM -
                                               ₃ħFyn
   DITIQQL VQHYIERAAG LCCRLAVPCPKGT-
                                               `cYrk****
221
   NSLQQLVAYYSKHADGLCHRLTTVCPTSK-
                                               hSrc
224
   DILOKI VKHYTEHADGLCHKLTTVCPTVKI-
                                               hYes
   NSVQELVQHYMEVNDGLCNLLIAPCTIMK-
                                               hFgr
   PCISDMIKHYQKQADGLCRRLEKACISPKI-
                                               hLyn
196 STLQELVDHYKKGNDGLCQKLSVPCMSSK-
                                               hHc k
   PGLHEL VRHYLINASDGLCIRLLS RPCOTOK-
                                               hLck
                                               mBlk
   PTLQALVQHYSKKGDGLCOKLTLPCVNLA-
   PAPFOLSYKTVDQWEIDRNSLQLLKRLGSG
                                               MKK3 MPI
                                                      aa
   PRLTDLSVKITKDVWEIPRESLOLIKRLGNG
                                               hFyn
   PKLADLSVKTKDVWEIPRESLQLLQKLGNG
                                                cYrk
250
   POTQGLA---KDAWEIPRESLIRLEVKLGQG
                                                hSrc
253
   |PQ|TQG|LA|---|KDAWEIPRESL|R|LE|V|KLG|Q|G
                                                hYes
260
   POITEGLA -- KDAWEISRSSITLERRLGTG
246
                                                hFqr
   PQ---KPWDKDAWEIPRESIKLVKRLGAG
                                                hLyn
231
   |PQ|---K|PW|E|KDAWEIPRESLKLEKKLGAG
                                                hHck
225
   PQ----KPWWEDEWEVPRETLKLVERLGAG
                                                hLck
229
   PK----NIWA QDEWEIPROSLKLIVRKLGSG
                                                m81k
   QFGEVWEGLWNNTTPVAVKTLKPGSMDPND
                                                MKK3 MPI
                                                       G G
   QFGEVWMGTWNGNTKVAIIKTLKPGTMSPE<u>ls</u>
                                                hF yn
281
   QFGEVWMGTWNGTT<u>K</u>VA<u>V</u>KTLKPGTMSPEA
                                                cYrk
280
   C|FGEVWMGTWNGTT|R|VA|I|KTLKPGTMSPEA
                                                hSrc
280
   C|FGEVWMGTWNGTTKVALIKTLKPGTMMPEA
                                                hYES
287
   CIF GDV WLIG T W N GST K V A V K T L K P G T M S P K A
                                                hFgr
273
   Q F G E V W M G Y Y N N S | T K V A V K T L K P G T M S | V Q | A
                                                hLyn
257
   Q F G E V W MATY NK H T K V A V K T M K P G S M S V E A
                                                hHck
251
   Q F G E V W M G Y Y N G H T K V A V K S L K Q G S M S P D A
                                                hLck
255
                                                mBlk
   Q F G E V W M G Y Y K N N M K V A T K T L K E G T M S P E A
   IF LIRIE A QI I M KINIL R HIPIK LII Q L Y A VIC T LIELDIP I Y
                                                MKK3 MPI
                                                       aa
274
   FLEEAQIIMKKLKHDKLVQLYAVVSI-EEPIY
                                                hFyn.
   FLEEAQLIMKRLRHDKLVQLYAVVS - EEPIY
                                                cYrk
310
   FLQEAQVMKKLRHEKLVQLYAVVS - EEPIY
                                                hSrc
310
    |FL|Q|EAQ||MK|K|LRHDKLV|PLYAVVS|-|EEPIY
                                                hYes
317
    |FLEEAQVMK|L|LRHDKLVQLYAVVS|-|EEPIY
                                                hFgr
303
    FLEE AN LIMKTLOHDKL VRILY AV VTREEPIY
                                                hLyn
287
                                                hHck
    IF LIAIE AINIVMKTLIQIHDKL VKILIHIA V VITKE PI Y
281
    FLAE AN LMKOLOHORL VRLYAVVIT - QEPIY
                                                hLck
285
     LIGE ANV MKTLIQHE RIL VRIL Y A V VIT RE-PIY
                                                mBlk
275
```

Title: NOVEL MEGAKARYOCYTIC PROTEIN 7 2 6 3 ... 0 6 0 7 0 E TYROSINE KINASES

```
I LITELIMIR HIG S LIQE Y LIQ ND TG SKI HL T Q Q V D
                                                      ∴MKK3 MPI
    I V T E Y M|N|K G S L L D F L K|D G|E G|R A|L K L P|N|L V D
340
    IVTEFMS QG S L L D F L K|D G D|G|R Y|L <u>K</u> L P Q L V D
                                                      cYrk
339
    | I V T E Y M | S K G S L L D F L K | G E T | G | K Y | L R L P Q L V D |
                                                      hSrc
339
    I V T E F M S K G S L L D F L K E G D G K Y L K L P Q L V D
                                                      hYes
346
    I <u>V</u> T E F M C H G S L L D F L K N P E G Q D L R L P Q L V D
                                                      hFqr
332
    I I I T E Y M A K G S L L D F L K S D E G G K V L L P K L I D
                                                      hLyn
317
    | | | | | | T E F M A K G S L L D F L K <u>S D E</u> G S K Q P L P K L I I D
                                                      hHck
310
     ITEYMENGSLVDFLKTPSGIKLTINKLLD
                                                      hLck
314
                                                      mBlk
     V T E Y M AR G C L L D F L K T D E G S R L S L
304
    MAAQVASGMAYLESRNYIHRDLAARNVLVG
                                                       MKK3 MPI
334
    MAAQVAAGMAYIERMNUIHRDLRSANILVG
                                                       hFyn
370
    |MAAQIA|A|G MAYIERMNY I HRDLRAAN I L V G
                                                       cYrk
369
    MAAQIASG MAYVERMNYVHRDLRAANIL V G
                                                       hSrc
369
    MAAQIADG MAYIERMNYIHRDLRAANIL V G
                                                       hYes
376
    MAAQVAEG MAYMERMNY I HRDLRAAN I L V G
                                                       hFgr
362
    F S A Q I A E G M A Y I E R K N Y I H R D L R A A N V L V S
                                                       hLyn
347
    F S A Q I A E G M A F I E Q R N Y I H R D L R A A N I L V S
                                                       hHck
340
    MAAQIAEGMAFIEERNYIHRDLRAANILVS
                                                       hLck
344
                                                       mBlk
    IMISIA QIVIA E G M A Y I E R M N S I H R D L R A A N I L
    EHNIYKVADFGLARVFKVDNEDIYES RHEI
                                                       MKK3 MPI
                                                               aa
364
    NGLLICKIADFGLARLI -- EDNEYTARQGA
                                                       hFyn
400
    DINL V C K I A D F G L A R L II - - - E D N E Y T A R Q G A
                                                       cYrk
399
    ENLVCK[V]ADFGLARLI|---|EDNEYTARQGA
                                                       hSrc
    ENLVCKIADFGLARLI|--- EDNEYTARQGA
                                                       hYes
406
    ERLACKIADFGLARLI --- KIDIDIE YN PCQGIS
                                                       hFgr
392
    ESLMCKIADFGLARVII -- EDNEYTAREGA
                                                       hLyn
377
    A S|L V C K I A D F G L A R V I | - - - |E D N E Y T A R | E | G A
                                                       hHck
370
    DTILSCKIADFGLARLII---EDNEYTAREGA
                                                       hLck
374
                                --- DISIE Y T A Q E G A
    |E|T|L|C|CKIADFGLARIII|-
                                                       mBlk
364
                                                       MKK3 MPI
    K L P V K W T A P E A I R S N K F S I K S D V W S F G I L L
                                                               aa
394
                                                       hF yn
427
    |KFPIKWTAPEAAL|Y|GRFTIKSDVWSFGILL
    KFPIKWTAPEAALFGKFTIKSDVWSFGILL
                                                       cYrk
426
    |KFPIKWTAPEAAL|Y|GRFTIKSDVWSFGILL
                                                       hSrc
426
    KFPIKWTAPEAAL|Y|GRFTIKSDVWSFGIL|Q
                                                       hYes
433
    K F P I K W T A P E A A L F G R F T I K S D V W S F G I L L
                                                       hFgr
419
    KFP1KWTAPEA [IN] FGC FT1KSDVWSFG1LL
                                                       hLyn
404
    KFPIKWTAPEA|IN|FG|S|FTIKSDVWSFGILL
                                                       hHck
397
    KFPIKWTAPEA|INYG|T|FTIKSDVWSFG<u>I</u>LL
                                                        hLck
 401
    K F P I K W T A P E A I H F G V F T I K A D V W S F G V L L
                                                        mBlk
```

MEGAKARYOCYTIC PROTEIN 977261 060702 TYROSINE KINASES



424 457 456 456 463 449 434 427 431 420	T E L V T K G R V P T E L V T K G R V P T E L T T K G R V P T E L V T K G R V P T E L I T K G R I P Y E I V T Y G R I P M E I V T Y G R I P	YPGMNNRE YPGMNNRE YPGMVNRE YPGMVNRE YPGMNKRE YPGMNKRE YPGRTNAD YPGMSNPE	VIQMLAQNYRLP VLEQVERGYRMP VLEQVERGYRMP VLEQVERGYRMP VLEQVERGYRMP VLEQVEQGYHMP VMTALSQGYRMP VIRALERGYRMP VIRALERGYRMP VIRSLEHGYRMP	MKK3 MPI hFyn cYrk hSrc hYes hFgr hLyn hHck hLck mBIk	ga
45.4 487 486 486 493 479 464 457 461 450	C P G G C P P S L F C P P E C P E S L F C P G G C P E S L F C P P G C P A S L Y R V E N C P D E L Y R P E N C P E E L Y R P D N C P E E L Y	I - E L M I H C W I - D V M V Q C W I - D L M C Q C W I - E L M N L C W I - E A M E Q T W I - D I M K M C W I - Q L M R L C W	NAEPKERPTFET KKDPEERPTFEY KREPEERPTFEY RKEPEERPTFEY KKDPDERPTFEY RLDPEERPTFEY KEKAEERPTFDY KNRPEERPTFEY KERPEDRPTFEY	MKK3 MPI hFyn cYrk hSrc hYes hFgr hLyn hHck hLck mBIk	00
483 516 515 515 522 508 493 486 490 480	L Q S F L E D Y F T L QAF L E D Y F T I Q S F L E D Y F	T A T E P Q Y Q P T A T E P Q Y Q P T S T E P Q Y Q P T A T E P Q Y Q P T A T E G Q Y Q Q T A T E G Q Y Q Q T A T E G Q Y Q Q T A T E G Q Y Q Q	G E N L G D N Q G E N L G D Q T D Q P D Q P	MKK3 MPI hFyn cYrk hSrc hYes hFgr hLyn hHck hLck mB1k	00

Title: NOVEL TOTAL
TYROSINE KINASES

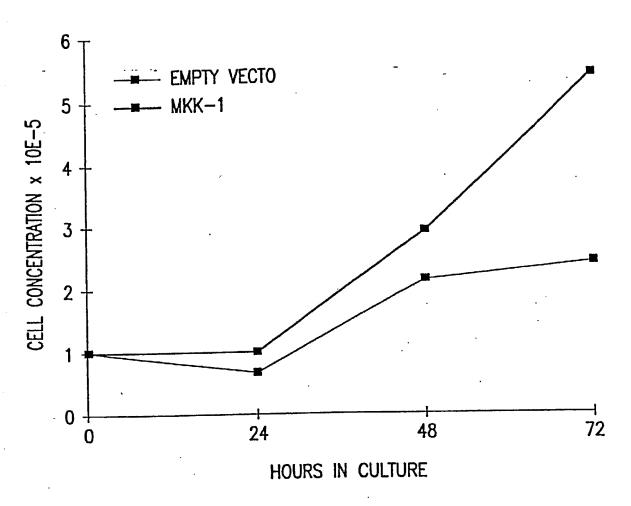


FIG.12

MEGAKARYOCYTIC PROTEINO 77261 .. 160702

TYROSINE KINASES Inventor(s): Axel ULLRICH et al.

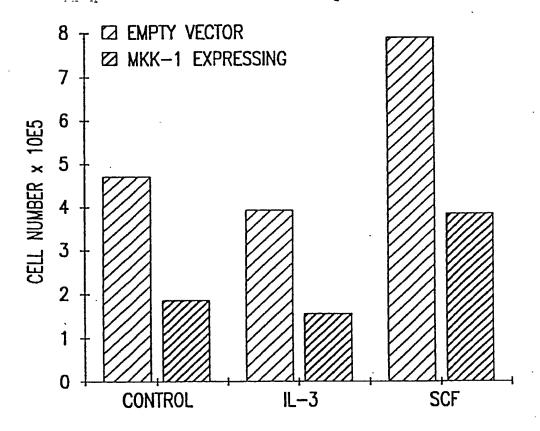


FIG.13

